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L4: Entry 1 of 39 File: USPT Jan 9, 2001

DOCUMENT-IDENTIFIER: US 6171799 B1
TITLE: Monoclonal antibodies reactive with defined regions of the T cell antigen receptor

DEPR:
In particular embodiments of the invention, a lymphatic malignancy or immune disorder may be diagnosed by detecting the immunospecific binding of a monoclonal antibody, or derivative or fragment thereof, reactive with an epitope of a defined constant or variable region of a T cell antigen receptor in a patient sample. The patient sample may consist of any body fluid, including but not limited to peripheral blood, plasma, cerebrospinal fluid, lymphatic fluid, peritoneal fluid, or pleural fluid, to name but a few, or any body tissue. Binding may be accomplished and/or detected in vitro or in vivo. In vitro binding may be performed using histologic specimens or subfractions of tissue or fluid, i.e. substantially purified T cells. In vivo binding may be achieved by administering the antibody or fragment or derivative by any means known in the art (including but not limited to intravenous, intraperitoneal, intranasal, and intrasarterial, to name but a few) such that immunospecific binding may be detected; for example, by attaching a radioactive label to the diagnostic antibody, fragment, or derivative.

DEPR:
Alternatively, according to the invention, a lymphatic malignancy or immune disorder may be diagnosed by detecting the presence of nucleic acid sequences homologous to a gene encoding a defined constant or variable region of a T cell antigen receptor in mRNA from a patient sample. Several procedures could be used to correlate TCR gene expression with disease. These involve 1) producing and analyzing cDNA libraries obtained from the disease related T cells to determine the presence of frequently used or dominant TCR genes. 2) Analyzing disease samples by Southern blot to determine whether specific genetic polymorphisms (restriction fragment length polymorphisms, RFLPs) or oligoclonal TCR rearrangements exist. 3) Analyzing disease samples by the cDNA synthesis, polymerase chain reaction amplification, and slot blot hybridization procedure, see Section 11, infra. The third procedure represents a moreeficient procedure in the time required for analysis and in the number of patients that can be analyzed to detect a disease correlation. A fourth procedure using in situ hybridization of T cells without prior T cell culturing may also be extremely useful. Once the disease correlations of interest have been identified, then specific TCR based therapeutics, e.g. anti-TCR monoclonal antibodies, may be

based therapeutics, e.g. anti-TCR monoclonal antibodies, may be produced (see 11.3 infra).

L4: Entry 2 of 39 File: USPT Oct 10, 2000

DOCUMENT-IDENTIFIER: US 6130071 A
TITLE: Vascular endothelial growth factor C (VEGF-C) .DELTA.Cys.sub.156 protein and gene, and uses thereof

BSPR:
In another aspect, the invention includes an antibody which is specifically reactive with one or more polypeptides of the invention, and/or is reactive with polypeptide multimers of the invention. Antibodies, both monoclonal and polyclonal, may be made against a polypeptide of the invention according to standard techniques in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1988)). Standard protein manipulation techniques and recombinant techniques also may be employed to generate humanized antibodies and antigen-binding antibody fragments and other chimeric antibody polypeptides, all of which are considered antibodies of the invention. The invention further includes hybridoma cells that produce antibodies of the invention or other cell types that have been genetically engineered to express antibody polypeptides of the invention. Antibodies of the invention may be used in diagnostic applications to monitor angiogenesis, vascularization, lymphatic vessels and their disease states, wound healing, or certain tumor cells, hematopoietic, or leukemia cells. The antibodies also may be used to block the ligand from activating its receptors; to purify polypeptides of the invention; and to assay fluids for the presence of polypeptides of the invention. The invention further includes immunological assays (including radio-immuno assays, enzyme linked immunosorbent assays, sandwich assays and the like) which employ antibodies of the invention.

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L6: Entry 1 of 3 File: USPT Oct 10, 2000

DOCUMENT-IDENTIFIER: US 6130071 A
TITLE: Vascular endothelial growth factor C (VEGF-C) .DELTA.Cys.sub.156 protein and gene, and uses thereof

ABPL:
Provided are purified and isolated VEGF-C cysteine deletion variants that bind to Flt4 receptor tyrosine kinase (VEGFR-3) but demonstrate reduced binding (relative to VEGF-C) to kdr receptor tyrosine kinase (VEGFR-2); polynucleotides encoding the polypeptide; vectors and host cells that embody the polynucleotides; pharmaceutical compositions and diagnostic reagents comprising the polypeptides; and methods of making and using the foregoing.

DEPR:
A 153 bp fragment encoding the 5' end of the Flt4 ligand was labeled with [.sup.32 P]-dCTP using the Klenow fragment of E. coli DNA polymerase I (Boehringer Mannheim). That fragment was used as a probe for hybridization screening of the amplified PC-3 cell cDNA library.

DEPR:
The conchae are surrounded with a rich vascular plexus, important in nasal physiology as a source for the mucus produced by the epithelial cells and for warming inhaled air. It is suggested that VEGF-C is important in the formation of the concheal venous plexus at the mucous membranes, and that it may also regulate the permeability of the vessels needed for the secretion of nasal mucus. Possibly, VEGF-C and its derivatives, and antagonists, could be used in the regulation of the turgor of the conchal tissue and mucous membranes and therefore the diameter of the upper respiratory tract, as well as the quantity and quality of mucus produced. These factors are of great clinical significance in inflammatory (including allergic) and infectious diseases of the upper respiratory tract. Accordingly, the invention contemplates the use of the materials of the invention, including VEGF-C, Flt4, and their derivatives, in methods of diagnosing and treating inflammatory and infectious conditions affecting the upper respiratory tract, including nasal structures.

DEPC:
Screening the PC-3 Cell CDNA Library Using the 5' PCR Fragment of Flt4 Ligand CDNA